REMARKS

The amendments to the specification are to correct obvious typographical errors.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings To Show Changes Made.**"

No new matter has been introduced by the amendments to the specification.

The amendment to the specification in the paragraph beginning on line 14 of p. 7 is to correct a typographical error. Specifically, at line 23 of p. 7, circumferential "stress" has been corrected to read circumferential --strain-- . Basis is prior usage of this terminology within the specification, such as, for example, at p. 2, lines 17 and 19.

The amendment to the specification in the paragraph beginning on page 15, line 18 is to clarify the description of embodiments of the present invention.

Specifically, the amendment clarifies that the embodiment shown in Fig. 1A comprises four actuators, while other embodiments may comprise a greater number of actuators. Because the basis for this amendment is Figs. 1A-1D, as filed with the application, applicant respectfully submits no new matter has been added.

The amendment to the specification in the paragraph beginning at page 14, line 1, is to clarify that a pressure sensor **18** can be placed in the external chamber **36** to monitor external chamber pressure. In the specification at p. 15, lines 5-11, applicant refers to pump P4 connecting to the external chamber **36**, and providing external pressure on the compliant vessel **12** contained therein. Although not all sensors **18** were shown in the drawings, it is inherent in an invention such as the present invention, where pressure is a major factor, that a sensor to monitor the external chamber pressure would be present. Applicant

respectfully submits that no new matter has been introduced by this amendment.

The amendment to the paragraph beginning at page 23, line 28, is to correct the description of the material used to prepare the vessel. Line 30 refers to this material as "silastic", which is incorrect, because SILASTIC® is a trademark, for a brand of silicone tubing. Line 26 of p. 23 correctly refers to the use of "silicone" tubing, and therefore, "silastic" in line 30 has been replaced with --silicone-- to describe this material correctly.

The amendment to the specification at the paragraph beginning at page 25, line 17, is to clarify that serum or other substances can be employed where they are under study or required. The use of serum has been described in the specification at p. 25, lines 6-9. One skilled in the art would recognize the use of serum and other substances as described by this amendment.

The amendment to the specification at p. 27, line 35 is to clarify the properties of the vessel models prepared in Example 1 of the specification (p. 23, line 26 - p. 24, line 29). While the model vessel was chosen for having a structure similar to that of actual human vessels, for the model system to have physiological meaning, one of ordinary skill in the art would realize it is inherent that the model vessel have material properties similar to actual human vessels. Properties of the various types of vessels which could be used are further described in Examples 7 and 8, at p. 27, line 33 - p.29, line 1 of the specification. No new matter has been introduced by this amendment.

Claims 2, 3, 4 and 6 have been amended.

Claim 2 has been amended to depend from added claim 11, instead of claim 1. Basis is Figs. 1A, 1B; p. 11, line 35 - p. 17, line 17.

Claim 3 has been amended to depend from added claim 11, instead of claim 1. Basis is p. 10, line 35 - p. 11, line 7; p. 13, line 28 - p. 14, line 8.

Claims 4 and 6 have been amended to clarify the language of the claim, wherein endothelial cells are the preferable choice for the blood vessel.

Basis is Example 2, at p. 24, line 31 - p. 25, line 28 of the specification.

Please add Claims 7-54, inclusive. These claims are being added to more fully define the invention. Because several of the originally filed claims now depend from the added claims, it was necessary to amend these original claims, and applicant respectfully submits that these amendments are not related to patentability.

The basis for the added Claims are summarized below:

Claim #(s):	**Basis:**
7, 33, 37, 38, 49, 51, 52, 53, 54	Figs. 1A, 1B; P. 15, lines 3-25.
8, 13, 39, 40	P. 16, lines 13-24.
9	Fig. 1A; P. 14, lines 10-19.
10	Figs. 1A, 1C; P. 12, lines 4-16.
11, 23, 24, 25, 26, 27, 28, 30, 31, 32	Figs. 1A, 1B; P. 11, line 35 - p. 17, line 17.
12	Figs. 1A, 1B; P. 15, lines 18-25.
14	P. 15, lines 18 - 25; p. 16, lines 22-24.
15	P. 15, lines 22-24, lines 31-35.
16	P. 15, lines 22-24.
17	Fig. 1A, 1B; P. 20, lines 3-19.
18, 44	Figs. 1A, 1C; P. 18, line 32 - p. 19, line 4.
19, 45	Figs. 1A, 1C; P. 12, lines 18-27.
20	Figs. 1A, 1C; P. 12, line 29 - p. 13, line 8.
21, 47	Figs. 1C, 1D; P. 18, lines 22-26.
22, 29, 36, 50	P. 23, lines 4-11; p. 23, lines 13-15; p. 23, line 28 - p. 24, line 29; p. 24, line 33 - p. 25, line 15; p. 27, line 35 - p. 28, line 18.
34, 35	Figs. 1A, 1C; P. 20, lines 3-19.
41, 42	P. 16, lines 13-24; p. 16, line 31- p. 17, line 12.
43	Figs. 1A, 1B; P. 12, lines 4-16.
46	Figs. 1A, 1C; Fig. 9; P. 12, line 29 - p. 13, line 8.

48 P. 20, lines 3-19; P. 13, lines 4-24.

Applicant respectfully submits that these Claims define patentable subject matter, and the Examiner is hereby requested to allow the present Claims.

In the event that this Amendment does not place the application in condition for allowance, the Examiner is respectfully requested to telephone the undersigned in order that an attempt can be made to place the application in condition for allowance as expeditiously as possible.

Respectfully submitted,

Mitchell P. Novick

MITCHELL P. NOVICK
Attorney for Applicant
Reg. No. 30,305

DATED: January 8, 2002

Law Offices of Mitchell P. Novick
66 Park Street
Montclair, New Jersey 07042
(973) 744-5150

MPN:BA/s
1626-1116

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	DANCU, MICHAEL et al.	Atty. Docket No:	1626-1116
Serial No:	09/973,433	Examiner:	(Unknown)
Filed:	October 8, 2001	Group Art Unit:	(Unknown)

For: SYSTEM AND METHOD TO SIMULATE HEMODYNAMICS

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 14 of page 31 has been amended as follows:

> The most common WSS simulating systems utilize a 2-dimensional stiff surface, such as a glass slide, for the endothelial cell culture forming the wall of a parallel plate flow chamber. The WSS in these devices is usually steady because of difficulties in simulating pulsatile flow. Cyclic straining devices provide only strain, by stretching cells on a compliant membrane without flow. Both types of systems are thus limited by their design. However, no studies have been performed studying both parameters (WSS and CS) using cells grown on a single type of support surface because such a

system, until now, has remained technologically unfeasible. The present invention addresses and solves this long-felt need by providing a system in which endothelial cells can be grown on a single support surface, and subjected to studies in wnicn both wall shear stress and circumferential strain ~~stress~~ can be examined independently of each other.

Paragraph beginning at line 18 of page 10 has been amended as follows:

The present invention is a system for hemodynamic simulation comprising ~~comprises~~ a vessel having properties of a blood vessel, a reservoir containing a quantity of fluid, tubing connecting the vessel and reservoir, and at least one pump for circulating the fluid within the system. Fluid can be tissue culture medium or blood analog fluid, and the vessel may include mammalian cells attached to its inside. A drive system, comprising two reciprocating drive shafts that are coupled by a cam, enables the uncoupling of pulsatile flow and pulsatile pressure to provide independent control over wall shear stress and circumferential strain. The shaft drives two pumps that are 180 degrees out-of-phase and are connected upstream and downstream of the vessel, and effect this uncoupling.

Paragraph beginning at line 18 of page 15 has been amended as follows:

Each of pumps **40** and **42** is under the control of a drive system unit **44**, which comprises a plurality of independent linear actuators **46**. These actuators **46** can be individual, stand alone units, for may be controlled by one or more computer systems **48**. In the embodiment in Fig. 1A, the second pumps **40** are connected by a shaft

50, and the third pumps 42 are connected by a second shaft 52. In one embodiment of the present invention, in which a 4-bar linkage mechanism is the drive system, a cam 54 affects the control of the various second pumps 40 and third pumps 42. In one embodiment of the present invention (Fig. 1B) the drive system unit 44 comprises six computer-controlled linear actuators~~.~~, while in another embodiment (Fig. 1A) the drive system unit 44 comprises four independent computer-controlled linear actuators.

The paragraph beginning at line 1 of page 14 has been amended as follows:

A pressure sensor 18 is used for monitoring the internal system pressure, and positioned either upstream and/or downstream of the compliant vessel 12. A pressure sensor can also be placed in the external chamber 36 to monitor external chamber pressure. Pressure sensor 18 can also be a blood pressure catheter (such as, for example, and not intended as a limitation, a MILLAR® catheter (MPC-500 with pressure meter TCB500; Registered Trademark of Millar Instruments Corp,, Houston TX), in either a fluid contacting or non-contacting version. Pressure sensor 18 may also be a pressure probe, such as those known to those skilled in the art. In one embodiment of the present invention, the pressure sensor is a catheter tip transducer (Millar) which is inserted upstream into the lumen of the compliant vessel. Where cells are being used in the compliant vessel 12, the pressure sensor 18 is kept upstream to avoid damaging the cells. Pressure drop across the compliant vessel has been shown to be negligible.--

Paragraph beginning at line 28 of page 23 has been amended as

follows:

In this example, the vessel chosen for growth of endothelial cells is a silicone ~~silastic~~ tubing, sold by Dow-Corning, Midland, MI under the brand name of SYLGARD 184® elastomer, or Silastic (MDX4-4210), Medical Grade tubing, and used to prepare elastic artery models. These models were prepared using the method described by Lee and Tarbell (1997, and hereby incorporated by reference), and included the preparation of models of human linear and bifurcating arteries.

The paragraph beginning at line 17, page 25 has been amended as follows:

Requirements of the fluid **16** include having a viscosity that can be elevated to achieve conditions of physiologic stress at modest flow rates. Dextran is used within the fluid while the present invention uses vessels of approximately 0.79 cm diameter; in instances employing vessels of smaller diameter, addition of dextran is not necessary. The fluid should be free of Phenol Red and serum so as not to interfere with measurements of other cellular products, such as prostacycline or nitric oxide. Serum and other substances can be added to the media if these substances are under study, or if the serum or substance is required by the cell line.

Paragraph beginning at line 35 of page 27 has been amended as follows:

Example 1 described the use of vessel models, modeled after the structure and material properties of actual human aortic vessels. In addition to using models of vessels, other vessels can be used in

conjunction with the present invention. These can be chosen from the group consisting of an artery, an artificial artery, a vein, human umbilical tissue, or a non-rigid tube. The artery may comprise a bovine aorta, or a human coronary artery. The vein may comprise bovine veins, or human veins such as a human leg vein or a human umbilical vein. Bovine tissue can be obtained from commercial supply sources, such as Vec Technologies, Ithaca NY and human umbilical materials can be obtained a local hospital, or a commercial sources such as Clonetics, Vec Technologies, or other sources known to those skilled in the art. In addition to studying the effects of hemodynamic conditions on endothelial cells, other types of cells can also be used, including smooth muscle cells, cartilage cells, osteocytes, embryonic and adult stem cells, and the like.

In the Claims:

2. (Amended) The system as described in claim 11~~1~~, wherein the vessel preferably is a model of a mammalian blood vessel.

3. (Amended) The system as described in claim 11~~2~~, wherein the vessel is biocompatible.

4. (Amended) The system as described in claim 2, wherein the vessel more preferably ~~further~~ comprises endothelial cells from a mammal.

6. (Amended) The method as described in claim 5, wherein the vessel more preferably ~~further~~ comprises endothelial cells from a mammal.

MPN:BA/s
1626-1116